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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,992	07/07/2000	Wen-Teng Wu	08415/003001	6577

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Y Rocky Tsao
Fish & Richardson P C
225 Franklin Street
Boston, MA 02110-2804

EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/611,992	WU ET AL.
	Examiner	Art Unit
	Ruth A. Davis	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Applicant's Request for Continued Examination and amendment have been received and entered into the case. Claims 29 – 31 have been added. Claims 1 – 31 are pending and have been considered on the merits. All arguments have been fully considered.

Claim Objections

Claim 29 is objected to because it is identical in scope to claim 4.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 – 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The phrase "full-grain particle solid substrate" was not described in the specification as originally filed. The specification does describe a nutritionally solid substrate defined as a solid, which keeps its solid morphology in a medium with examples

drawn to rice particles and rice powder. However, there is not adequate support for a "full-grain" or whole piece of rice as instantly claimed.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 – 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 – 31 are drawn to a method for culturing filamentous fungi, however are rendered vague and indefinite for reciting "full-grain particle solid substrate" because the phrase is not adequately defined by the specification. The phrase "full-grain" appears inconsistent with a "particle" solid substrate. For example, it is unclear how one could have an entire piece of grain and a particle of the grain at the same time.

The phrase is further confusing because it is unclear if "full-grain" is defining the grain itself (i.e. a whole piece of grain) or that the grain is nutritionally sound (i.e. as used with "whole wheat").

In claim 4, line 1, "the carbohydrate" lacks sufficient antecedent basis. It would appear that the claim should rather depend from claim 3. For purposes of examination, the claim has been interpreted to depend from claim 3.

Claims 13, 21 and their dependent are rendered vague and indefinite for reciting "by using a full grain particle solid substrate" because the claims do not set forth any steps involved

in the "use of" the substrate. Moreover, it is unclear what method/process applicant is intending to encompass.

Claim 27 is confusing because it depends on claim 20, which recites the same limitations. It would appear that the claim should rather depend from claim 21. For purposes of examination, the claim has been interpreted to depend from claim 21.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 – 4, 13, 21 and 29 – 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Bayer et al. (US 5013655).

Applicant claims a method for cultivating filamentous fungi, the method comprises preparing a medium comprising a full grain particle solid substrate and inoculating the medium with the filamentous fungi, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate. The filamentous fungi comprises Monascus, Penicillium or Aspergillus, the substrate is a carbohydrate, specifically rice. Applicant additionally claims a method for producing metabolites from culturing Monascus species, the method comprising preparing medium comprising a full grain particle solid substrate and inoculating the medium with the

Monascus species, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate.

Bayer et al. teaches a method for obtaining colorants (metabolites) from Monascus species wherein Monascus are fermented in fluidized bed reactors (pneumatic reactors) (abstract) on solid rice, wherein the rice allows the fungi to attach (col.2 line 47-51).

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 – 4, 6, 13, 21 and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bayer in view of Johal.

Applicant claims a method for cultivating filamentous fungi, the method comprising preparing a medium comprising a full grain particle solid substrate and inoculating the medium with the filamentous fungi, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate. The filamentous fungi comprises Monascus, Penicillium or Aspergillus, the substrate is a carbohydrate, specifically rice. The medium further comprises a nitrogen source, inorganic salts and trace elements. Applicant additionally claims the method for cultivating Monascus species, and for producing metabolites from culturing Monascus species.

Bayer et al. teaches a method for obtaining colorants (metabolites) from Monascus species wherein Monascus are fermented in fluidized bed reactors (pneumatic reactors) (abstract) on solid rice, wherein the rice allows the fungi to attach (col.2 line 47-51).

Bayer does not teach the method wherein the medium further comprises a nitrogen source, inorganic salts and trace elements. However, Johal teaches that typical methods of culturing filamentous fungi include mediums containing a nitrogen source, inorganic salts and trace elements (col.4 line 29-35). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Johal to add a nitrogen source, inorganic salts and trace elements to the medium of Bayer because of its well known and common use as disclosed by Johal.

10. Claims 1 – 5, 7 – 8, 13 – 16, 21 – 23 and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haas et al. (US 4031250).

Applicant claims a method for cultivating filamentous fungi, the method comprising preparing a medium comprising a full grain particle solid substrate and inoculating the medium with the filamentous fungi, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate. The filamentous fungi comprises Monascus, Penicillium or Aspergillus, the substrate is a carbohydrate, specifically rice. The method further comprises steps of husking, cocking and sterilizing the rice before adding it to the medium. In addition, the fungi are cultured before being inoculated into the medium. Culturing comprises inoculating the filamentous fungi from a stock to a new agar plate, incubating for 5 – 7 days, washing spores and mycelia that were grown with sterile water, and cultivating the obtained spores and mycelia in a medium comprising a full grain solid substrate for 36 – 48 hours by shaking. Applicant additionally claims the method for producing metabolites from culturing Monascus species, the method comprising preparing medium comprising a full grain particle solid substrate and inoculating the medium with the Monascus species, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate.

Hass et al. teaches a method for producing pigments (metabolites) from culturing Monascus purpureus on rice or corn (abstract). The method comprises starting with a stock culture of Monascus, culturing the fungi on agar slants (col.1 line 55-63), washing the slants (or spores and mycelia that were grown) with water (col.2 line5-13), followed by inoculation into the sterilized rice and/or corn medium (col.1 line 64-68, col.2 line 12-13). Haas also teaches that such inoculations may be used to inoculate further batches of rice and/or corn (col.2 line 13-16).

Although Haas does not specifically teach the rice and/or corn is in full grain form, the reference does teach grinding, crushing and flaking the rice before adding it to foods (col.2 line

58-65). This suggests that the rice and/or corn are, in fact, "full grain" or whole, while acting as the substrate for the Monascus culture.

In addition, Haas does not specifically teach the method wherein the cultivation takes place within a bioreactor. However, at the time of the claimed invention, it was well known in the art that filamentous fungi such as Monascus were routinely cultured in bioreactors. In support, Johal et al. (US 4954440) teaches culturing Monascus in bioreactors for their metabolites (abstract) and Yamaguchi et al. (US 3765906) teaches culturing Monascus in jar fermentors (bioreactors) for their pigments (examples 1 – 4). As such, it would have been obvious to one of ordinary skill in the art to practice the methods of Hass in a bioreactor because it was routine practice in the art at the time the claimed invention was made.

Finally, Hass does not teach that the rice and/or corn is husked and cocked before use, or the specific incubation, fermentation and culture times as claimed. However, it would have been obvious to one of ordinary skill in the art to use husked corn and cocked rice before practicing the methods of Haas, since such steps would have already been performed before the methods of Haas could be practiced. In addition, it would have been obvious to one of ordinary skill in the art to optimize such times as it was routinely practiced in the art at the time of the claimed invention. Moreover, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to modify and determine optimal incubation, fermentation and culture periods when practicing the methods of Haas.

11. Claims 1 – 4, 7 – 10, 13, 15 – 17, 21, 23 – 26 and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hass in view of Bayer and Tung et al. (1997).

Applicant claims a method for cultivating filamentous fungi, the method comprising preparing a medium comprising a full grain particle solid substrate and inoculating the medium with the filamentous fungi, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate. The filamentous fungi comprises Monascus, Penicillium or Aspergillus, the substrate is a carbohydrate, specifically rice. The fungi are cultured before being inoculated into the medium. Culturing comprises inoculating the filamentous fungi from a stock to a new agar plate, incubating for 5 – 7 days, washing spores and mycelia that were grown with sterile water, and cultivating the obtained spores and mycelia in a medium comprising a full grain solid substrate for 36 – 48 hours by shaking. Further, the bioreactor is a pneumatic bioreactor with an airlift and net draft tube. Applicant additionally claims the method for producing metabolites from culturing Monascus species, the method comprising preparing medium comprising a full grain particle solid substrate and inoculating the medium with the Monascus species, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate.

Hass et al. teaches a method for producing pigments (metabolites) from culturing Monascus purpureus on rice or corn (abstract). The method comprises starting with a stock culture of Monascus, culturing the fungi on agar slants (col.1 line 55-63), washing the slants (or spores and mycelia that were grown) with water (col.2 line5-13), followed by inoculation into the sterilized rice and/or corn medium (col.1 line 64-68, col.2 line 12-13). Haas also teaches that such inoculations may be used to inoculate further batches of rice and/or corn (col.2 line 13-16).

Although Haas does not specifically teach the rice and/or corn is in full grain form, the reference does teach grinding, crushing and flaking the rice before adding it to foods (col.2 line

58-65). This suggests that the rice and/or corn are, in fact, "full grain" or whole, while acting as the substrate for the Monascus culture.

Haas does not teach the method wherein the Monascus are cultured in a pneumatic bioreactor with an airlift and net draft tube. However, at the time of the claimed invention, it was well known in the art that filamentous fungi such as Monascus were routinely cultured in bioreactors. In support, Bayer teaches culturing Monascus in fluidized bed reactors with bubble columns (abstract, col.2 line 40-45) (or pneumatic bioreactors with airlifts) for obtaining pigments, Johal teaches culturing Monascus in bioreactors for their metabolites (abstract) and Yamaguchi teaches culturing Monascus in jar fermentors (bioreactors) for pigments (examples 1 – 4). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to practice the methods of Hass in a bioreactor because it was routine practice in the art at the time the claimed invention was made. Furthermore, at the time of the claimed invention, pneumatic bioreactors with airlift and net draft tubes were known in the art. Bayer teaches culturing Monascus in pneumatic bioreactors with airlifts wherein the fungi were cultured on rice and metabolites are obtained (col.2 line 40-60). In addition, Tung et al. teaches that airlift reactors with net draft tubes have been used in fermentation (p.1). Specifically, the airlift bioreactors with net draft tubes are disclosed to provide higher gas hold up, smaller bubbles, lower mixing times and shorten fermentation times (abstract). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Bayer and Tung to use an airlift bioreactor with net draft tubes in the methods of Hass for their known use and disclosed benefits as cited above.

Finally, Hass does not teach the specific incubation, fermentation and culture times as claimed. However, it would have been obvious to one of ordinary skill in the art to optimize such times as it was routinely practiced in the art at the time of the claimed invention. Moreover, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to modify and determine optimal incubation, fermentation and culture periods when practicing the methods of Haas.

12. Claims 1 – 4, 6, 11 – 13, 19 – 21 and 27 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hass in view of Johal.

Applicant claims a method for cultivating filamentous fungi, the method comprising preparing a medium comprising a full grain particle solid substrate and inoculating the medium with the filamentous fungi, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate. The filamentous fungi comprises Monascus, Penicillium or Aspergillus, the substrate is a carbohydrate, specifically rice. The medium further comprises a nitrogen source, inorganic salts and trace elements. The method further comprises cultivating the fungi using the fed batch process with a medium comprising a nitrogen source and full grain solid substrate. Applicant additionally claims the method for producing metabolites from culturing Monascus species, the method comprising preparing medium comprising a full grain particle solid substrate and inoculating the medium with the Monascus species, in a bioreactor for fermentation, wherein the mycelia attach to the solid substrate.

Hass et al. teaches a method for producing pigments (metabolites) from culturing Monascus purpureus on rice or corn (abstract). The method comprises inoculating Monascus into a medium comprising sterilized rice and/or corn (col.1 line 64-68, col.2 line 12-13).

Although Haas does not specifically teach the rice and/or corn is in full grain form, the reference does teach grinding, crushing and flaking the rice before adding it to foods (col.2 line 58-65). This suggests that the rice and/or corn are, in fact, "full grain" or whole, while acting as the substrate for the Monascus culture.

In addition, Haas does not specifically teach the method wherein the cultivation takes place within a bioreactor. However, at the time of the claimed invention, it was well known in the art that filamentous fungi such as Monascus were routinely cultured in bioreactors. In support, Johal teaches culturing Monascus in bioreactors for their metabolites (abstract) and Yamaguchi et al. teaches culturing Monascus in jar fermentors (bioreactors) for their pigments (examples 1 - 4). As such, it would have been obvious to one of ordinary skill in the art to practice the methods of Hass in a bioreactor because it was routine practice in the art at the time the claimed invention was made.

Haas does not teach the method wherein the medium further comprises a nitrogen source, inorganic salts and trace elements; or wherein the fungi are cultivated via fed-batch with a medium comprising nitrogen and full grain solid substrate. However, Johal teaches that typical methods of culturing filamentous fungi include fed batch fermentation in bioreactors (col.3 line25-35) with mediums containing a nitrogen source, inorganic salts and trace elements (col.4 line 29-35). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Johal to culture the filamentous fungi via fed batch with a nitrogen source,

inorganic salts and trace elements in the medium because of its well known and common use as disclosed by Johal.

Response to Arguments

Applicant argues that the references do not teach full, whole grains as solid substrates in the methods of culturing filamentous fungi and that the whole, solid substrates produce higher pigmentation yields. However, these arguments fail to persuade in light of the rejections above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
July 12, 2002